PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:
MICHAEL A. RODRIGUEZ
GUERIN & RODRIGUEZ, LLP
5 MOUNT ROYAL AVENUE
MOUNT ROYAL OFFICE PARK
MARLBOROUGH, MA 01752

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing (*day/month/year*)	12 JUL 2005
Applicant's or agent's file reference SRI-008PC	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date (*day/month/year*)	Priority date (*day/month/year*)
PCT/US05/02033	21 January 2005 (21.01.2005)	23 January 2004 (23.01.2004)

International Patent Classification (IPC) or both national classification and IPC

IPC(7): B01L 3/00, 3/02; G01N 21/29, 25/22, 21/00, 1/10 and US Cl.: 422/99, 100, 82.05, 930; 436/157, 164, 180

Applicant

SRI INTERNATIONAL

1. This opinion contains indications relating to the following items:

- ☒ Box No. I — Basis of the opinion
- ☐ Box No. II — Priority
- ☐ Box No. III — Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV — Lack of unity of invention
- ☒ Box No. V — Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI — Certain documents cited
- ☐ Box No. VII — Certain defects in the international application
- ☐ Box No. VIII — Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(*b*) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US	Authorized officer
Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Brian Gordon Telephone No. (571) 272-1700

Form PCT/ISA/237 (cover sheet) (January 2004)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US05/02033

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☐ in computer readable form

c. time of filing/furnishing

☐ contained in international application as filed.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US05/02033

Box No. V Reasoned statement under Rule 43 *bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims 4-9, 11, 13-21, 23-28, 30, 32-36	YES
	Claims 1-3, 10, 12, 22, 29, 31	NO
Inventive step (IS)	Claims 4-9,11, 13-21, 23-28, 30, and 32-36	YES
	Claims 1-3, 10, 12, 22, 29, 31	NO
Industrial applicability (IA)	Claims 1-36	YES
	Claims NONE	NO

2. Citations and explanations:

Please See Continuation Sheet

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US05/02033

Supplemental Box
In case the space in any of the preceding boxes is not sufficient.

V. 2. Citations and Explanations:
Claim 22 and 29 lacks novelty under PCT Article 33(2) as being anticipated by Sasaki et al. US 2003/0086824.

Sasaki et al. diclsoscs when a plate for the flat cell transmits measuring light to a certain extent, measurement is carried out by the use of the transmittance or the absorbance calculated on the basis of the transmittance. Specifically, measuring light 8 emitted by a light source 7 passes through the droplet on the hydrophilic pattern and the plate and a portion thereof is absorbed by them. The unabsorbed light 9 reaches a light receptor 10. A specific component in the sample is quantitated from the attenuation factor of the measuring light at a measuring wavelength. When a plate for the flat cell reflects measuring light to a certain extent, measurement is carried out by the use of the reflectance. Specifically, measuring light 12 emitted by a light source 11 passes through the droplet on the hydrophilic pattern, is reflected from the cell surface and passes through the droplet (droplet on surface) on the hydrophilic pattern again. In this process, a portion of the measuring light is absorbed by the droplet and the cell surface. The unabsorbed light, i.e., light 13 that has been reflected from the cell surface and has again passed through the droplet on the hydrophilic pattern reaches a light receptor 14. A specific component in the sample is quantitated from the attenuation factor of the measuring light at a measuring wavelength. See [0045]

Claim 22 and 29 lacks novelty under PCT Article 33(2) as being anticipated by Hess et al. US 2002/0001544 A1.

Hess et al. dicloses at least one operation may be performed on each droplet from the group of operations consisting of mixing, diluting, concentrating, filtering, and analyzing. Analyzing may include performing at least one operation from the group of operations consisting of optical interrogation and mass spectrometry. Optical interrogation may include at least one of fluorescence spectrometry, Raman spectroscopy and UV absorption. Analyzing the content of each droplet may include aspirating each droplet into a dispensing unit and presenting each droplet for analysis via the dispensing unit. Each droplet may be presented to a mass spectrometer and a characteristic of each droplet determined by means of mass spectrometry. Analyzing a characteristic of each droplet may include heating each droplet, or applying a pneumatic or explosive force to each droplet, so as to form an atomized spray and determining a characteristic each droplet by means of mass spectrometry. Each droplet may be vibrated so as to cause atomization, whereupon a characteristic of each droplet can be determined by means of mass spectrometry. Vibrating the droplet may include focusing a pulsed laser (light source) onto the surface or backside of the surface in a proximity of each droplet, utilizing acoustic waves, or mechanically vibrating the surface. A voltage to the surface onto which each droplet is deposited may be applied to assist in the formation of atomized spray. See [0009]

Claim 22 and 29 novelty under PCT Article 33(2) as being anticipated by Anderson et al. US 6,620,620.

Anderson et al. disclose in FIGS. 2A and 2B illustrate the arrangements used in the droplet sensing method known as video drop sensing. Droplet 42 is deposited from needle 36 of syringe 34 onto deposition surface plate 44. Light source 66 directs light through light diffuser 68, droplet 42 and optional diffuser 70 to video camera 72. As shown in FIG. 2B, video screen 74 (which may be a component of display 24) includes crosshairs 76 which are movable by controls 26 so as to permit the operator to determine a change in the light obscuration as the droplet evaporates. Video camera 72 is interfaced with the power, logic and computing module 22 shown in FIG. 1 so that a change in light obscuration due to the evaporation of at least a portion of the liquid or solvent permits the next successive droplet to be deposited in a timely manner. In a preferred embodiment, a blue or other colored filter may be used to improve the sensitivity of the video camera, and a blunt end needle may be used to improve the wetting of the droplet to the needle.

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US05/02033

Supplemental Box
In case the space in any of the preceding boxes is not sufficient.

FIG. 3 is a visual representation of the sensing of the evaporative process by means of the change in a reflected laser beam. Droplet 42 is deposited from needle 36 of syringe 34 onto deposition surface plate 44. Laser 78 directs a laser beam at the droplet on deposition surface plate 44, which beam is reflected toward detector 80. When the liquid or solvent droplet has not yet fully evaporated, the reflected beam is scattered and the detector 80 does not yet receive the full beam. Detector 80 is interfaced with the power, logic, and computing module 22 shown in FIG. 1 so that a change in the spectral distribution of the reflected laser beam due to the evaporation of at least a portion of the liquid or solvent permits the next successive droplet to be deposited in a timely manner.

Claims 1, 3, 10, 12, 22, 29 and 31 novelty under PCT Article 33(2) as being anticipated by Yuguchi et al. US 5,275,787.

Yuguchi et al. discloses In FIGS. 9 and 10, a fixed transparent glass plate 16 is arranged tilted relative to the discharge axis l of the nozzle 1. The laser beam emitted from the laser light source 7 is incident from the back of the glass plate 16. The discharge axis l of the nozzle 1 and the optical axis O of the laser light are arranged so as to cross near the glass plate 16. The detector 5 is arranged on the optical axis of the laser light. A condenser lens (not shown) and a beam stopper (not shown) for preventing the laser beam from directly entering the detector 5 are provided in front of the detector 5 on the optical axis. The condenser lens and beam stopper form a dark-field optical system so that light scattered in forward directions of the optical axis by a particle S situated at a measuring position on the glass plate 16 onto which the laser beam is projected is subjected to photometry by the detector 5. The detector 6 is arranged in a direction crossing each of the optical axis O of the laser light and the axis l of the liquid drop discharge. A condenser lens (not shown) and the wavelength selection filter 15 are provided in front of the detector 6 so that fluorescence emitted from the particle S at the measuring position is selectively subjected to photometry by the detector 6.

The size of the opening and the capacity of the heater are set so that the liquid drops discharged from the nozzle have diameters of about 50 μm-80 μm.

Claims 22 and 29 novelty under PCT Article 33(2) as being anticipated by Krause et al. US 5,586,200.

Krause et al. teach a system for measuring sample volumes of droplets using a rod-like transfer element. The light of lamp (1) is split into two beams (2) and (3) with each beam being directed onto the sample adhering to the transfer element (4) via a system of lenses, diaphragms, and mirrors. The axis of a rod-like transfer element runs perpendicularly to the drawing surface. The light beams (2) and (3) consequently illuminate the sample droplets from two perpendicular directions which in turn run perpendicularly to the axis of the transfer element. The illuminated sample droplet is located in the focus of the lens systems (5) and (6) by which it is imaged in such a way that a sharp picture is generated on the CCD-camera (8). The bundles of beams emerging from the lens systems (5) and (6) pass through an arrangement of mirrors, diaphragms, and lenses. The semi-permeable mirror (7) directs the partial beams onto the CCD-camera (8).

Claims 4-9, 11, 13-21, 23-28, 30, and 32-36 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest and immiscible organic liquid that controls evporration, a second immiscible liquid, a thermal gradient in the immiscible liquid, and a dye droplet in the immiscible liquid.

Claims 1-36 meet the criteria set out in PCT Article 33(4), and thus meet industrial applicability because the subject matter claimed can be made or used in industry.